REMARKS

Upon entry of this amendment, claims 14 and 45-54 are pending in the instant application. Claims 36-44 are canceled herein. Applicant reserves the right to prosecute the canceled subject matter, as well as the originally presented claims, in continuing applications. Claims 14, 50, 52 and 53 have been amended herein.

Support for the claim amendments presented herein is found throughout the specification and in the claims as originally filed. For example, support for the transporter peptides recited in amended claim 14 is found at least at pg. 23, lines 20-25; at pg. 24, lines 3-5; at pg. 24, lines 10-15; at pg. 24, lines 19-20; and at pg. 25, lines 3-5. Finally, support for the additional step of detecting translocation recited by amended claims 50 and 53 is found at least at pg. 9, lines 20-25; at pg. 11, lines 22-26; at pg.16, lines 20-21; at pg.16, lines 20-27; at pg. 16, line 31 through pg. 17, line 5; at pg. 20, lines 13 – 32; and at pg. 24, lines 19 - 20.

Accordingly, no new matter has been added by these amendments.

I. Response to Office Communication

In the Office Communication mailed April 28, 2004, the Examiner asserted that Applicant's January 30, 2004 response to the September 30, 2003 office action was not fully responsive. For the following reasons, Applicant contends this response is fully responsive to the September 30, 2003 office action.

a) Claim 50

The Examiner asserts that claims 50-54, submitted with the January 30, 2004 response, are directed to an invention that is independent or distinct from the invention originally claimed. Claims 50-54 recited a "method of detecting translocation of a transporter peptide across the membrane," which the Examiner asserted is distinct from the "method of translocating a transporter peptide" elected for prosecution in the Response to Restriction Requirement filed on July 15, 2003. These claims have been amended herein to address the Examiner's rejection.

Claim 50 has been amended to depend on claim 14, which recites the method of translocating a transporter peptide. Claim 50 now recites the additional step of detecting the

presence of a transporter peptide inside a B-cell after contacting the pancreatic B-cell with a transporter peptide. Rather than reciting a method of detecting translocation of a transporter peptide, the amended claim provides an additional step to the method of translocating the transporter peptide. Thus, Applicant contends that these claims fall within the invention that was elected in the Response to the Restriction Requirement filed on July 15, 2003.

Applicant also contends that the additional step recited by amended claim 50 and claims 51-54, which depend therefrom, are supported by the as-filed specification. More specifically, the specification describes several ways of detecting translocation when translocating a transporter peptide such as biochemical, immunohistochemical and fluorescent labeling. First, the specification discloses a biochemical method of detection wherein B-cells incubated with phage-bearing peptides were removed, the B-cells were harvested and lysed to release the internalized phages, and the transporter peptides displayed by the internalized phages were sequenced. (*See* specification at pg. 21, lines 24-27). This step was used to detect transporter peptides with SEQ ID NOs: 1, 2, 3 and 6.

Second, the specification describes an immunohistochemical means of detecting wherein, following the contacting step, internalized phages displaying transporter peptides were visualized in B-cells by treating the B-cells with an antibody directed to the phage capsid and then treating the cells with a fluorescein-conjugated antibody directed to the first antibody allowing visualization of internalized phage-bearing peptides by fluorescence microscopy. (*See* specification at pg. 21, line 31 through pg. 22, line 4).

Finally, the specification discloses a detecting step whereby the transporter peptides are themselves fluorescently labeled for visualization by fluorescence microscopy (*See* specification at pg. 24 lines 15-20). More specifically, a transporter peptide of SEQ ID NO:1 was linked to a 10-amino acid random sequence labeled with FITC in order to detect translocation after the contacting step. While the FITC-labeled transporter peptides were visualized in B-cells, the labeled transporter peptides were not visualized in other cell types. In light of the support in the specification, Applicant contends that the specification as-filed supports claims 50-54.

b) Claim 14

The Examiner noted that claim 14, as amended in the January 30, 2004 Response, is directed to a transporter peptide of formula $X_mRX_oRX_n$, differs in scope from the original claim

14, which is drawn to transporter peptides selected from the group consisting of SEQ ID NOs: 1-6. The claims have been amended herein to address the Examiner's rejection.

As amended herein claim 14 now recites a method of translocating a transporter peptide into a pancreatic B-cell, involving contacting a pancreatic B-cell with a transporter peptide for a time and under conditions sufficient to allow a transporter peptide to translocate across a membrane of the B-cell, wherein the transporter peptide comprises the amino acid sequence of SEQ ID NO:1. Since the claims have been amended to recite one specific transporter peptide selected from the group consisting of SEQ ID NOs: 1-6, Applicant contends claim 14 as amended is the proper scope.

The Examiner found that the January 30, 2004 amended claim 14 was non-responsive to the September 30, 2003 Office Action, since the elected species of SEQ ID NO:1 does not read on the amended transporter polypeptide of formula $X_mRX_oRX_n$. Claim 14 now recites a method of translocating a transporter peptide comprising SEQ ID NO:1 into a pancreatic B-cell. Consequently, the elected species of SEQ ID NO:1 reads on the transporter peptide of claim 14, as amended herein. As a result, Applicant contends claim 14, as amended herein, is responsive to the office action.

II. CLAIM REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH

The Examiner asserts that "[t]he specification does not disclose the method of translocating a transporter peptide across the membrane of pancreatic B-cells." Office Action pg. 4. The claims have been amended herein to address the Examiner's rejection. Claim 14 now recites a method of translocating a transporter peptide into a pancreatic B-cell, involving contacting a pancreatic B-cell with a transporter peptide comprising the amino acid sequence of SEQ ID NO: 1 for a time and under conditions sufficient to allow a transporter peptide to translocate across a B-cell membrane.

Applicant contends that the specification fully supports the method of amended claim 14. For contacting a B-cell *in vitro*, the specification as-filed discloses a method whereby transporter peptides are "...incubated with cells at a temperature which enables active metabolism of the cells" or that the transporter peptide can be "...injected into particular cells." (*See* specification at pg. 10, lines 29-32). The specification also discloses a method whereby phage-bearing,

randomized peptide sequences were added to B-cell cultures and allowed to incubate. During incubation, phage-bearing peptides contacted B-cells resulting in the translocation across a B-cell membrane and enrichment of particular phage-bearing peptides. After several cycles of contact and enrichment, the peptides were characterized. As shown in Table 2, the phage-bearing transporter peptides of SEQ ID NOs: 1, 2 and 3 translocated a B-cell membrane by this method. (*See* specification at pg. 27, lines 20-25).

Additionally, the specification as-filed also provides specific examples of methods of translocating a B-cell membrane with transporter peptides. In particular, the specification discloses a time-sequence titration experiment documenting the time-dependent, increased translocation of the phage-bearing transporter peptide of SEQ ID NO:1 across a B-cell membrane by use of this method. (*See* specification at pg. 24, lines 1-5). The specification also describes cell specificity experiments in which phage-bearing transporter peptides of SEQ ID NO:1 translocated across a B-cell membrane, by use of this method, 10,000- to 100,000-fold more efficiently than the same peptides translocated across other cell membranes. (*See* specification at pg. 24, lines 10-15). Further, the specification describes a method of translocating a B-cell membrane by contacting B-cells with detectably-labeled transporter peptides. More specifically, the method involved contacting B-cells with a FITC-labeled peptides by incubation. After incubation, fluorescence microscopy revealed that the transporter peptide with SEQ NO:1 translocated a B-cell membrane in an amount sufficient to create a signal, whereas the same transporter peptide contacting other cell types did not translocate the cell membrane in an amount sufficient to generate a signal. Consequently, Applicant asserts that the specification as-filed provides disclosure of methods of translocating a transporter peptide across a B-cell membrane as recited in amended claim 14.

Second, the Examiner asserts that "[t]he specification disclosure does not disclose the use of peptides with SEQ ID NOs: 2-6 in the claimed method." Office Action pg. 4. The claims have been amended to address the Examiner's rejection. As previously discussed, the claims have been amended herein to recite a method of translocating a transporter peptide across a B-cell membrane by contacting a B-cell with a transporter peptide comprising the amino acid sequence of SEQ ID NO: 1. Consequently, the rejection is moot and should be withdrawn.

Third, the Examiner asserts that "the invention lacks showing of sufficient identifying characteristics or lacks examples of the transporter peptides of SEQ ID NOs 2-6 in the claimed method to demonstrate possession of the claimed generic[sic]." Office Action pg. 4. The claims have been amended to address the Examiner's rejection. As previously discussed, the claims have been amended herein to recite a method of translocating a transporter peptide across a B-cell membrane by contacting a B-cell with a transporter peptide comprising the amino acid sequence of SEQ ID NO: 1. Thus, the rejection is moot and should be withdrawn.

Finally, the Examiner asserts that "the sequences with SEQ ID NOs: 4 and 5 do not share or have the required convertase consensus RXXR, such that the assertion of that the peptides with SEQ ID NOS 4 and 5 are also transporter peptides [sic] ." As previously discussed, the claims have been amended herein to recite a method of translocating a transporter peptide across a B-cell membrane by contacting a B-cell with a transporter peptide comprising the amino acid sequence of SEQ ID NO: 1. Claim 14 as amended no longer encompasses the peptides of SEQ NOs: 4 and 5. Therefore, the rejection is moot and should be withdrawn.

III. Claim Rejections Under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claim 14 under 35 U.S.C. §112, second paragraph as being indefinite. According to the Examiner, claim 14 fails to particularly point out and distinctly claim the subject matter regarded as the invention. Applicant notes claim 14 has been amended herein to recite a method translocating a transporter peptide into a pancreatic B-cell by contacting with a transporter peptide under conditions sufficient to permit translocation of a B-cell membrane. Further, Applicant contends that claim 14 as amended is not indefinite because it contains clear limitations that are supported by the specification. (*see, e.g.*, specification at pg. 21, lines 17-22)

Second, the Examiner has rejected claim 14 under 35 U.S.C. §112, second paragraph as being incomplete for omitting essential steps. In particular, the Examiner has asserted that claim 14 does not recite how the transporter peptides are translocated across the membrane of pancreatic B-cells. As discussed above, claim 14 has been amended herein to recite the method steps for translocating a transporter peptide into a pancreatic B-cell. Applicant contends,

therefore, that the pending claims do not omit any essential steps. As a result, Applicant requests the Examiner withdraw this rejection.

CONCLUSION

On the basis of the foregoing amendments, Applicant respectfully submits that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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